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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,665	06/28/2004	Arturo Leone	206,588	3094

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EXAMINER	
STOICA, ELLY GERALD	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,665	LEONE ET AL.	
	Examiner	Art Unit	
	Elly-Gerald Stoica	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-62* is/are pending in the application.

4a) Of the above claim(s) *34,39-45 and 54-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-33,35-38,46-53 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/25/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Invention I, Claims 30-33, 35-38, 46-53, and 62, as drawn to antibodies that recognize BAG 3 protein and fragments thereof selected from the following Seq. Id. Nos.: 15, 16, 17, 18, in the reply filed on 04/27/2007 is acknowledged. The traversal is on the ground that in the previous PCT prosecution the issue of the lack of unity of the invention had not been raised. This is not found persuasive because the argument does not prove that unity of Invention is lacking and the position of the Office, as presented in the previous Office action, is that the claims of this National stage entry application lack unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

Status of the claims

2. Claims 30-62 are pending. Claims 34, 39-45, 54-61 were withdrawn. Claims 30-33, 35-38, 46-53, and 62, as drawn to antibodies that recognize BAG 3 protein and fragments thereof selected from the following Seq. Id. Nos.: 15, 16, 17, 18 are currently examined.

Claim objections

3. Claims 30, 31, 48, 53 are objected to for containing non-elected subject matter. Specifically, the claims contain, in their recitations, references to the non-elected Seq. Id. Nos.: 2, 4, 6, and 8.

Claims 30, 31, 33, 35, 38, 48, 52, 53 are objected to for the wording "selected in the group", which should read "selected from the group".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 31 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to protein or fragments of it having at least 75%, 80%, 90%, 95%, and 98% homology to at least one of the polypeptides selected from the group of sequences identified as Seq. Id. Nos.: 15, 16, 17, 18, or functional equivalents of them. The claims do not require that the polypeptides possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of peptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics

of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of polypeptide species (Seq. Id. Nos.: 15, 16, 17, 18) is not adequate written description of an entire genus of functionally equivalent polypeptides which incorporate all variants and fragments and with at least 75%, 80%, 90%, 95%, and 98% sequence homology to a peptide selected from the group of sequences identified as Seq. Id. Nos.: 15, 16, 17, 18, or functional equivalents of them.

The remaining 2-25% of the protein or peptide is not described until its reduction to practice. For instance the existence of BAG3 proteins of another specie that might be part of the BAG3 genus has to be first discovered and thus its description and possession is not adequate until reduction to practice. While the written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function, if the Applicant intends to claim antibodies that bind to specific epitopes and these epitopes are within the sequence disclosed (i.e. in the percentile of the genus claimed) that would constitute adequate written description. However, because of the breadth of the claims, the

capability to recognize or understand the structure from the mere recitation of percentage homology to the respective peptides of Seq. Id. Nos.: 15, 16, 17, 18, or functional equivalents of them is highly unlikely. In this case, disclosure of function alone (i.e., peptides recognized by isolated antibodies) is little more than a wish for possession; it does not satisfy the written description requirement. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406 (written description requirement not satisfied by merely providing "a result that one might achieve if one made that invention"); In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming a rejection for lack of written description because the specification does "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). See also< Tronzo v. Biomet, 156 F.3d at 1159, 47 USPQ2d at 1833 (Fed. Cir. 1998), >wherein< the disclosure of a species in the parent application did not suffice to provide written description support for the genus in the child application.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of the sequences referred to above (Seq. Id. Nos.: 15, 16, 17, 18) the skilled artisan cannot envision the detailed chemical structure of the

encompassed peptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Therefore, only claims related to the Seq. Id. Nos.: 15, 16, 17, 18, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

6. Claims 30-33, 35-38, 46-53, and 62, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to antibodies that recognize or modulate BAG3 protein and fragments thereof characterized in that they are used in research, diagnostics and therapy for cell death-involving diseases, and for the modulation of cell survival and/or death, said protein and fragments being selected from the group of peptide sequences identified as SEQ ID NO: 15, 16, 17, 18. The antibodies are intended for use in the treatment of a disease selected from the group of: acute or chronic tissue damages, such as heart, kidney, brain or other organ ischemia, HIV- related damage of brain or other tissues, skeletal muscle disorders, transplantation rejection; chronic degenerative disorders such as Parkinson's disease, amyotrophic lateral sclerosis and others; and neoplastic, autoimmune and other diseases involving excessive or defective apoptosis; tissue repair or wound healing, treatment of surgical incisions, and ulcers, such as stomach or diabetic ulcers.

The state of the art, at the time that the invention was made, recognizes the use of specific antibodies for specific diseases, as evidenced by the prior art cited by Applicant. However, for the antibody-based therapy, the use of each antibody in the method of treatment would be a lengthy, unpredictable and extremely experimentation intensive process. The specification does not present any working example of the use of the antibodies claimed in modulation of cell survival in vitro, let alone the more complicated methods of use in vivo for diagnosis and/or treatment. The Applicant claims the use of the antibodies in a very broad category of diseases with various etiologies that, in the best-case scenario, share, sometime in the evolution of the disease, various aspects of an apoptotic process. However, the specification does not offer any guidance

as to the specific conditions actually treated or diagnosed. This lack of guidance is also questionable for the process of diagnosis, since the relationship between the BAG-3 protein and the numerous, unrelated diseases claimed is not established either in the specification or the prior art. The amount of experimentation needed to use the antibodies as claimed is considered undue and therefore the specification is not enabling for the invention as claimed.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-33, 35-38, 46-53, and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 as an independent claim, contains the wording: "Isolated antibodies that ... modulate BAG3 protein...". The meaning of the wording "modulate" in the context of an action from an antibody is unclear, i.e., do the antibodies stimulate or inhibit the protein?

The claim 38 contains the words: 'map constructs". It is not clear what is meant by these words. Is it a map (i.e. a diagram) or does it refer to Multiple Antigen Peptide construct? Is it a method of making antibodies or a protein that is used to make antibodies?

Claim 53 is indefinite because it is not clear what will the diagnostic agent will diagnose and thus the meets and bounds of the claim could not be established.

Claim 62 is indefinite because it is not clear what the meaning of the words: "functional equivalents" is.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 30-33, 46, 49-52 and 62 are rejected under 35 U.S.C. 102(e) as being anticipated by Reed et al. (U.S. Pat. 6,696,558).

The claims are drawn to antibodies that recognize or modulate BAG3 protein and fragments thereof characterized in that they are used in research, diagnostics and therapy for cell death-involving diseases, and for the modulation of cell survival and/or death, said protein and fragments being selected in the group of peptide sequences identified as SEQ ID NO: 15, 16, 17, 18. The antibodies are part of a composition or a kit.

Reed et al discloses antibodies specific for the human BAG family protein including polyclonal and monoclonal antibodies that retain binding activity, or chimeric antibodies or humanized antibodies. The polypeptide of Seq. Id. No: 20 used by Reed

et al to obtain the antibodies is the mature BAG3 polypeptide and the fragments of Seq. Id. Nos.: 15, 16, 17, 18 of the instant application are comprised in the sequence presented by Reed et al as presented infra. Non-naturally occurring antibodies can be constructed using solid phase peptide synthesis, can be produced recombinantly or can be obtained, for example, by screening combinatorial libraries consisting of variable heavy chains and variable light chains. Such peptide antibodies may be raised against any BAG domain of any of the human BAG proteins (col. 11, lines 32-62). The antibodies would necessarily have all the binding and functional properties conferred by the epitope that they are raised against. Hence all their properties are inherent and their use is not the patentability-determining factor.

Seq. Id. No: 15 of the current application is identical with the amino acids 18-33 of the Seq. Id. No.: 20 in the Reed et al patent (which is the human BAG-3 amino acid sequence).

Seq. Id. No: 16 of the current application is identical with the amino acids 389-399 of the Seq. Id. No.: 20 in the Reed et al. patent (which is the human BAG-3 amino acid sequence).

Seq. Id. No: 17 of the current application is identical with the amino acids 533-547 of the Seq. Id. No.: 20 in the Reed et al. patent (which is the human BAG-3 amino acid sequence).

Seq. Id. No: 18 of the current application is identical with the amino acids 561-575 of the Seq. Id. No.: 20 in the Reed et al. patent (which is the human BAG-3 amino acid sequence).

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-33, 46, 49-52 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Kohn et al. (U.S. Pat. 5, 652,223).

The claims are presented supra. Kohn et al teach antibodies against the Carboxyamido triazole (CAI) resistance protein (CAIR-1) (Seq. Id. No: 2). The fragments of Seq. Id. Nos.: 16, 17, 18 of the instant application are comprised in the sequence presented by Kohn et al., as presented infra. The antibody may be raised against synthetic peptides made using CAIR-1 sequences. Either monoclonal or polyclonal antibodies were generated, for subsequent use in immunoassays to measure the protein (col. 18, line 22 to col. 19 line 9). Kohn et al. also teach kits for detecting the presence of CAIR proteins in tissue or blood samples which comprise a container containing antibodies selectively immunoreactive to the protein and instructional material for performing the test. The kit may also contain other components such as CAIR proteins, controls, buffer solutions, and secondary antibodies (col. 21, lies 1-6).

The antibodies are part of a pharmacological composition that may be administered to a patient in an amount sufficient to block expression of CAIR proteins or to block particular signal transduction pathways. The amino acid sequence of the CAIR-1 is identical, less 2 conservative substitutions (Q227K and Q237R), to the BAG-3

amino acid sequence as evidenced by the Doong et al. reference (p. 4386, the paragraph bridging the left to right columns) (Oncogene, 2000, 19, 4385-4395), provided by the Applicant. The mutations are not part of the sequence 15-18 of the instant application.

Seq. Id. No: 16 of the current application is identical with the amino acids 51-65 of the Seq. Id. No.: 2 in the Kohn et al. patent.

Seq. Id. No: 17 of the current application is identical with the amino acids 199-213 of the Seq. Id. No.: 2 in the Kohn et al. patent.

Seq. Id. No: 18 of the current application is identical with the amino acids 227-241 of the Seq. Id. No.: 2 in the Kohn et al. patent.

The antibodies would necessarily have all the binding and functional properties conferred by the epitope that they raised against. Hence all their properties are inherent and their use is not the patentability-determining factor.

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elly-Gerald Stoica whose telephone number is (571) 272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eileen B. O'Hara

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